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**In the Claims**

Please cancel claim 31 and add new claim 89 and 90 as indicated in the listing of claims below pursuant to 37 C.F.R. §1.121.

1. (Original) Isolated nuclear protein which binds, in a sequence specific manner, to a transcriptional regulatory DNA element of an immunoglobulin light chain genes, a transcriptional regulatory DNA element of an immunoglobulin heavy chain genes or both.
2. (Original) Isolated nuclear protein, which binds, in a sequence specific manner, to enhancer DNA sequences of the kappa light chain gene.
3. (Original) A nuclear protein of claim 2, wherein the sequences are TGGGGATTCCCA.
4. (Original) Isolated NF- $\kappa$ B.
5. (Original) Isolated nuclear protein, which:
  - a) binds to DNA sequences in the upstream region of both mouse heavy and Kappa light chain gene promoters; and
  - b) binds to DNA sequences of mouse heavy chain gene enhancer.
6. (Original) A nuclear protein of Claim 5, wherein the sequences are ATTTGCAT.
7. (Original) Isolated nucleic acid encoding a nuclear protein of Claim 1.
8. (Original) Isolated nucleic acid encoding a nuclear protein which binds, in a sequence specific manner, to enhancer DNA

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sequences of the Kappa light chain gene.

9. (Original) Isolated nucleic acid of Claim 8 wherein the nuclear protein binds, in a sequence specific manner , to enhancer DNA sequences of the Kappa light chain gene.
10. (Original) Isolated DNA encoding a structural gene for a nuclear protein, which protein binds in a sequence specific manner to the kappa enhancer.
11. (Original) Isolated DNA which encodes a nuclear protein which:
  - a) binds to DNA sequences in the upstream region of both mouse heavy and Kappa light chain gene promoters; and
  - b) binds to DNA sequences of mouse heavy chain gene enhancer.
12. (Original) DNA encoding the transcriptional regulatory factor IgNF-B (NF-A2).
13. (Original) A cloned DNA sequence which encodes a protein which binds to the  $\kappa$ -element TGGGGATTCCCCA and which hybridizes to a single, approximate 10kb RNA transcript from both B and non-B human cells.
14. (Original) An assay for detection of binding of cellular nuclear protein to DNA, comprising the steps of:
  - a) providing an extract of cellular nuclear protein;
  - b) preparing an incubation mixture consisting of:
    - i) the extract of nuclear protein;
    - ii) a radiolabeled DNA fragment to be tested for binding with the nuclear protein; and
    - iii) an alternating copolymer duplex poly(dI-dc)-

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poly(dI-dc);

- c) incubating the mixture under conditions which allow the formation of protein-DNA complexes; and
  - d) resolving complexed DNA from free DNA by electrophoresis through a low ionic strength, nondenaturing polyacrylamide gel.
15. (Original) An assay of Claim 14, wherein the radiolabeled DNA fragment to be tested is less than about 100 base pairs.
16. (Original) A method of Claim 14, wherein the DNA fragment is end-labeled with <sup>32</sup>P.
17. (Original) A method of enhancing the transcription of a gene of interest whose transcription is regulated by a regulatory factor which binds DNA in the vicinity of the gene, comprising the steps of:
- a) preparing an expressible gene construct comprising a strong promoter linked to a gene encoding the regulatory factor; and
  - b) incorporating into a cell containing the gene of interest, single or multiple copies of the gene construct sufficient to enhance transcription of the gene of interest.
18. (Original) A method of Claim 17, wherein the cell is a lymphoid cell and the gene of interest is a gene encoding an Ig chain.
19. (Original) A method of Claim 17, wherein the regulatory factor is selected from the group consisting of the following factors: IgNF-A, E, IgNFB and NF-κB.

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20. (Original) A method of Claim 17, wherein the regulatory factor is IgNF-B.
21. (Original) A method of Claim 17, wherein the lymphoid cell is a hybridoma cell.
22. (Original) A method of enhancing transcription of a gene encoding an Ig chain, comprising:
  - a) preparing an expressible gene construct comprising a strong promoter linked to DNA encoding a structural gene for B-cell nuclear protein, which protein binds in a sequence specific manner to a transcriptional regulatory DNA element of an immunoglobulin light chain genes, a transcriptional regulatory DNA element of an immunoglobulin heavy chain gene or both; and
  - b) transferring an Ig chain-producing lymphoid cell with the construct in multiple copies to enhance the transcription of the Ig chain-encoding gene.
23. (Original) A method of claim 22, wherein the DNA encoding the structural gene for a B-cell nuclear protein encodes IgNFB.
24. (Original) A lymphoid cell transformed with an expressible nucleic acid construct comprising nucleic acid encoding a transcriptional regulatory factor which regulates Ig gene transcription.
25. (Original) A lymphoid cell of claim 24, which is a hybridoma.
26. (Original) A lymphoid cell of claim 24, wherein the regulatory factor is B-cell nuclear protein, which protein



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binds in a sequence specific manner to a transcriptional regulatory DNA element of an immunoglobulin light chain gene, a transcriptional regulatory element of an immunoglobulin heavy chain gene, or both.

27. (Original) A lymphoid cell of claim 26, wherein the regulatory factor is IgNF-B or NF- $\kappa$ B.
28. (Original) A method of screening for the expression of a sequence-specific binding protein by a recombinant expression vector, comprising contacting protein produced by a host cell transformed by the recombinant vector with a nucleic acid recognition site probe, under conditions which permit the specific formation of a complex of the sequence-specific binding protein and the recognition site probe and determining whether such formation of a complex occurs, wherein formation of a complex is an indication of the expression of the sequence-specific binding protein by the recombinant vector.
29. (Original) A method of identifying recombinant expression vectors which express a sequence-specific DNA binding protein, comprising the steps of:
  - a) cloning the vector in host cells to form clonal colonies'
  - b) generating a replica plate of the cellular protein of the clonal colonies;
  - c) contacting the cellular protein with a DNA probe comprising a DNA sequence embodying the binding site of the sequence-specific binding protein under conditions which permit the sequence specific binding protein to bind the probe to form a complex; and
  - d) washing the cellular protein to remove unbound probe.

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30. (Original) A method of claim 29, wherein the sequence-specific binding protein is a transcriptional regulatory factor.
31. (Canceled)
32. (Original) A method of claim 29, wherein a nonspecific competitor DNA is contacted with cellular protein along with the DNA probe.
33. (Original) A method of claim 32, wherein the nonspecific competitor DNA is poly(dI-dC)-poly(dI-dC) or denatured calf thymus DNA.
34. (Original) A method of claim 29, wherein the probe is up to 150 bp in length.
35. (Original) A method of claim 29, wherein the probe comprises a oligomer of binding sites for the sequence-specific binding protein.
36. (Original) A labeled DNA probe complementary to at least a portion the sequence of nucleic acid encoding a transcriptional regulatory factor.
37. (Original) A DNA probe of claim 36, wherein the factor is lymphoid-specific.
38. (Original) A DNA probe of claim 37, selected from the group consisting of NF- $\kappa$ B and IgNF-B.
39. (Original) A method of detecting DNA or RNA encoding a

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transcriptional regulatory factor, comprising contacting a sample to be tested with a labeled DNA probe complementary to at least a portion the sequence of nucleic acid encoding a transcriptional regulatory factor; incubating the probe and the sample under hybridization conditions which permit the labeled probe to hybridize with complementary DNA or RNA sequences; removing unhybridized probe and analyzing the sample for hybridized probe.

40. (Original) A method of claim 39, for determination of expression of the factor, wherein the conditions of hybridization are sufficiently stringent such that the probe hybridizes only to nucleic acid sequences to which it is substantially complementary.
41. (Original) A method of claim 39, for the identification of a gene encoding a transcriptional regulatory factor, wherein the hybridization conditions are of a sufficiently relaxed stringency such that the probe will hybridize to DNA sequences which are not completely complementary.
42. (Original) Polyclonal or monoclonal antibody specifically reactive with a nuclear protein which binds, in a sequence specific manner, to a transcriptional regulatory DNA element of an immunoglobulin light chain gene, a transcriptional regulatory DNA element of an immunoglobulin heavy chain gene or both.
43. (Original) An immunoassay for detection of a transcriptional regulatory factor in a biological fluid, in which the antibody of claim 42 is used to detect the transcriptional regulatory factor.

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44. (Original) An immunoassay of claim 43, for detection of IgNF-B or NF- $\kappa$ B, wherein the antibody is specifically reactive with IgNF-B or NF- $\kappa$ B.
45. (Original) The recombinant phage \h3, ATCC 67629.
46. (Original) The recombinant phage OCT-2, ATCC 67630.
47. (Original) A method of identifying an agonist or an antagonist of gene transcription, comprising employing a gene encoding a transcriptional regulatory factor in an in vivo or in vitro assay to identify an agonist or antagonist of the factor or the gene encoding the factor.
48. (Original) An agonist or antagonist of the activity of a transcriptional regulatory factor of claim 1 or a gene encoding the factor.
49. (Original) DNA encoding the DNA binding domain of a transcriptional regulatory protein of claim 1.
50. (Original) A method of specifically stimulating gene transcription in a cell, comprising:
  - a) providing an expressible gene construct comprising DNA encoding the binding domain of a transcriptional regulatory factor linked to DNA encoding an activator of the RNA polymerase for the gene; and
  - b) introducing the construct into the cell.
51. (Original) A method of claim 50, wherein the DNA encodes the binding domain of IgNF-B or NF- $\kappa$ B.
52. (Original) A DNA construct comprising DNA encoding the

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binding domain of a transcriptional regulatory factor linked to DNA encoding an activator of the Rna polymerase of the gene.

53. (Original) A DNA construct of claim 52, wherein the DNA encodes the binding domain of IgNF-B or NF- $\kappa$ B.
54. (Original) A method of inducing expression of a gene, comprising the steps of:
  - a) preparing a DNA construct comprising:
    - i) a Kappa enhancer sequence or a portion of the Kappa enhancer sequence containing at least the sequence to which the factor NF- $\kappa$ B binds;
    - ii) a promoter; and
    - iii) a structural gene of interest.
  - b) transfecting a eukaryotic host cell with the DNA construct; and
  - c) stimulating the transfected cell with a substance which stimulates NF-B activation and binding to the enhancer sequence.
55. (Original) A method of claim 54, wherein the structural gene encodes a cytotoxic protein.
56. (Original) A method of claim 54, wherein the substance which stimulates NF-B is an activator of protein kinase C.
57. (Original) A method of altering expression in a cell of a gene whose transcriptional activity is altered by binding of NF- $\kappa$ B to the enhancer of said gene, comprising controlling dissociation of the NF- $\kappa$ B-I $\kappa$ B complex present in the cytoplasm of said cell.

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58. (Original) The method of reducing expression in a cell of a gene whose transcriptional activity is activated by binding of NF- $\kappa$ B to the enhancer of said gene, comprising preventing dissociation of NF- $\kappa$ B-I $\kappa$ B complex present in the cytoplasm of said cell.
59. (Original) A method of activating in a host cell an NF- $\kappa$ B precursor present in the cytoplasm of said host cell, the precursor comprising an NF- $\kappa$ B-I $\kappa$ B complex, comprising contacting the host cell with a substance which causes dissociation of the complex into I $\kappa$ B and translocation of said NF- $\kappa$ B into the nucleus of said cell.
60. (Original) A method of preventing activation in a host cell of an NF- $\kappa$ B precursor present in the cytoplasm of said host cell, the precursor comprising an NF- $\kappa$ B-I $\kappa$ B complex, comprising contacting the host cell with a substance which prevents dissociation of the complex into I $\kappa$ B and NF- $\kappa$ B.
61. (Original) A method of causing activation of an NF- $\kappa$ B precursor, present in the cytosol of a host cell, the NF- $\kappa$ B precursor being an NF- $\kappa$ B-I $\kappa$ B complex, comprising treating the cell with a substance which causes dissociation of the NF- $\kappa$ B complex, resulting in induction of DNA-binding activity and nuclear translocation of the NF- $\kappa$ B present in the complex.
62. (Original) A method of controlling expression of human immunodeficiency virus DNA in a host cell latently infected with human immunodeficiency virus DNA, comprising preventing binding of NF- $\kappa$ B to human immunodeficiency virus transcriptional control elements.

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63. (Original) A method of claim 62 wherein binding of NF- $\kappa$ B to immunodeficiency virus transcriptional control elements is prevented by inhibiting dissociation of an NF- $\kappa$ B-I $\kappa$ B complex present in the cytoplasm of said host cell into I $\kappa$ B and NF- $\kappa$ B.
64. (Original) Isolated NF- $\kappa$ B-I $\kappa$ B complex.
65. (Original) Isolated DNA encoding NF- $\kappa$ B-I $\kappa$ B complex.
66. (Original) A method of regulating NF- $\kappa$ B-mediated gene expression in a cell, comprising altering NF- $\kappa$ B activity in the cell.
67. (Original) A method of regulating transduction in a cell of an extracellular signal by NF- $\kappa$ B, comprising altering NF- $\kappa$ B activity in the cell.
68. (Original) A method of claim 67 wherein NF- $\kappa$ B activity is reduced.
69. (Original) A method of claim 67 wherein NF- $\kappa$ B is enhanced.
70. (Original) A method of regulating NF- $\kappa$ B-mediated expression of a selected gene in a cell, comprising introducing into the cell a substance which regulates NF- $\kappa$ B activity in the cell.
71. (Original) A method of positively regulating NF- $\kappa$ B-mediated gene expression in a cell, comprising:
  - a) introducing into the cell a gene construct comprising a gene of interest, a DNA sequence which is the binding site of NF- $\kappa$ B and a promoter for the gene; and

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b) maintaining the cell under conditions appropriate for expression of the gene.

72. (Original) A method of claim 71 wherein the binding site is represented by the following consensus sequence:

C C  
GGGRATYYAC  
T T

or equivalents thereof.

73. (Original) A method of claim 72 wherein the consensus sequence is present in the group consisting of: the Ig  $\kappa$  enhancer regulatory element, the SV40 enhancer regulatory element, the HIV long terminal repeat, a regulatory element of the MHC class I H2-K gene, a regulatory element of the IL-2 lymphokine gene, a regulatory element of the IL-2R gene, and a regulatory element of the interferon  $\beta$  PRDII gene.

74. (Original) A method of positively regulating the expression of a gene in a cell, the gene having a DNA sequence which is a binding site of NF- $\kappa$ B, said method comprising introducing an effective amount of NF- $\kappa$ B into the cell, under conditions appropriate for binding of NF- $\kappa$ B to the binding site.

75. (Original) A method of positively regulating in a cell the expression of a gene comprising a DNA sequence which is a binding site of NF- $\kappa$ B, comprising introducing into the cell a gene construct encoding NF- $\kappa$ B and maintaining the cell, under conditions appropriate for expression of the gene.

76. (Original) A method of positively regulating the expression



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of a gene in a cell, the gene having a DNA sequence encoding a binding site of NF- $\kappa$ B, said method comprising inducing NF- $\kappa$ B activity by introducing into the cell an NF- $\kappa$ B inducing substance.

77. (Original) A method of claim 76 wherein the NF- $\kappa$ B inducing substance is selected from the group consisting of lipopolysaccharide, cyclohexamide, phorbol esters, virus, and tumor necrosis factor  $\alpha$  phorbol myristate.
78. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a binding site of NF- $\kappa$ B, said method comprising introducing an inhibitor of NF- $\kappa$ B into the cell, under conditions appropriate for binding of the inhibitor NF- $\kappa$ B.
79. (Original) A method of claim 78 wherein the inhibitor of NF- $\kappa$ B is I- $\kappa$ B.
80. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a binding site of NF- $\kappa$ B, said method comprising introducing a gene construct encoding I- $\kappa$ B cell, under conditions appropriate for I- $\kappa$ B production and binding of I- $\kappa$ B to NF- $\kappa$ B.
81. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a binding site of NF- $\kappa$ B, said method comprising introducing into the cell a DNA sequence which is the binding site of NF- $\kappa$ B, under conditions appropriate for binding of the DNA sequence and NF- $\kappa$ B.
82. (Original) A method of claim 81 wherein the binding site is

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represented by the following consensus of:

C C  
GGGRATYYAC,  
T T

or equivalents thereof.

83. (Original) A method of claim 81 wherein the consensus sequence is present in the group consisting of: the Ig  $\kappa$  enhancer regulatory element, the SV40 enhancer regulatory element, the HIV long terminal repeat, a regulatory element of the MHC class I H2-K gene, a regulatory element of the IL-2 lymphokine gene, a regulatory element of the IL-2R gene, and a regulatory element of the interferon  $\beta$  PRDII gene.
84. (Original) A method of modifying the expression of at least one gene in a cell, the gene having an NF- $\kappa$ B binding site, said method comprising introducing into the cell a gene construct comprising DNA encoding a modified NF- $\kappa$ B molecule which binds selectively to the NF- $\kappa$ B binding site of said selected gene or genes, under conditions appropriate for expression of the encoded modified NF- $\kappa$ B and binding of the modified NF- $\kappa$ B to the NF- $\kappa$ B binding site of said gene or genes.
85. (Original) A method of negatively regulating the expression of a gene in a cell, the gene having a DNA sequence encoding a binding site of NF- $\kappa$ B, said method comprising introducing into the cell a gene construct, the construct comprising DNA encoding a modified NF- $\kappa$ B molecule which comprises a DNA binding domain and lacks a RNA polymerase activating domain.

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86. (Original) Isolated or recombinant I $\kappa$ B.
87. (Original) A composition comprising an NF- $\kappa$ B inhibitor.
88. (Original) A composition of claim 85 wherein the inhibitor is a peptide capable of binding NF- $\kappa$ B.
89. (New) A method for reducing expression in a human cell of a gene, the expression of which has been induced by an external influence that activates NF- $\kappa$ B to act as an intracellular messenger to transmit a signal that induces expression of the gene from the plasma membrane of the cell to the nucleus of the cell, which method comprises within the cell inhibiting transmission of the signal so as to thereby reduce expression of the gene in the cell.
90. (New) A method for reducing expression in a human cell of a gene, the expression of which has been induced by an external influence that activates NF- $\kappa$ B to act as an intracellular messenger to transmit a signal that induces expression of the gene in the cell, which method comprises within the cell inhibiting transmission of the signal so as to thereby reduce expression of the gene in the cell.

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**REMARKS**

Claims 1-88 were pending in the subject application. By this Amendment, applicants have canceled claim 31 and added new claims 89 and 90.

Support for new claims 89 and 90 may be found, *inter alia*, on page 8, lines 1-7; on page 27, lines 17-20; and on page 8, line 16 to page 9, line 9 of the subject application.

**Restriction Requirement**

In the March 28, 2006 Restriction Requirement, the Examiner required restriction to one of the following allegedly distinct inventions as follows:

- I. Claims 1-4, drawn to isolated nuclear proteins which bind to transcriptional regulatory DNA elements of immunoglobulin genes;
  - I.
- II. Claims 5-6, drawn to isolated nuclear proteins which bind to DNA sequences upstream of both mouse heavy kappa light chain gene promoters and binds to mouse heavy chain gene enhancer;
- III. Claims 7-9, and 49 drawn to isolated nucleic acids encoding nuclear proteins which bind to transcriptional regulatory DNA elements of immunoglobulin genes;
- IV. Claim 10, drawn to isolated DNA encoding a structural gene for a nuclear protein which binds in a sequence specific manner to the kappa enhancer;
- V. Claims 11-12, drawn to isolated DNA which encodes a nuclear

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protein which binds to DNAs in the upstream region of both mouse heavy and kappa light chain gene promoters and binds to DNA sequences of mouse heavy chain gene enhancer;

VI. Claim 13, drawn to a cloned DNA sequence which encodes a protein which binds to TGGGGATTCCCA and hybridizes to a 10kb RNA transcript from both B and non-B human cells;

VII. Claims 14-16, drawn to an assay for detection of binding of cellular nuclear protein to DNA;

VIII. Claims 17-23, drawn to a method of enhancing the transcription of a gene of interest whose transcription is regulated by a regulatory factor which binds DNA in the vicinity of a gene;

IX. Claims 24-27, drawn to lymphoid cells;

X. Claim 28, drawn to a method of screening for the expression of a sequence-specific binding protein by a recombinant expression vector;

XI. Claims 29-35, drawn to a method of identifying recombinant expression vectors;

XII. Claims 36-41, drawn to DNA probes and methods of detecting DNA or RNA;

XIII. Claims 42-44, drawn to polyclonal or monoclonal antibodies and an immunoassay;

XIV. Claim 45, drawn to phage lambda h3, ATCC 67629;

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- XV. Claim 46, drawn to phage OCT-2, ATCC 67630;
- XVI. Claim 47, drawn to a method of identifying an agonist of gene transcription;
- XVII. Claims 48, and 87-88, drawn to an agonist or antagonist of nuclear proteins which bind to transcriptional regulatory DNA elements of immunoglobulin genes;
- XVIII. Claims 50-53, drawn to a method of specifically stimulating gene transcription in a cell;
- XIX. Claims 54-56, drawn to a method of inducing expression of a gene;
- XX. Claims 57-61, drawn to a method of altering expression in a cell of a gene whose transcriptional activity is altered by binding of NF- $\kappa$ B to the enhancer of said gene;
- XXI. Claims 62-63, drawn to a method of controlling expression of HIV DNA in a host cell;
- XXII. Claim 64, drawn to an isolated NF- $\kappa$ B - I $\kappa$ B complex;
- XXIII. Claim 65, drawn to isolated DNA encoding NF- $\kappa$ B - I $\kappa$ B complex;
- XXIV. Claims 66-73, drawn to a method of regulating NF- $\kappa$ B mediated gene expression in a cell;
- XXV. Claims 74-77, drawn to a method of positively regulating the expression of a gene in a cell;

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XXVI. Claims 78-83, drawn to a method of negatively regulating the expression of a gene in a cell;

XXVII. Claims 84-85, drawn to a method of modifying the expression of at least one gene in a cell, the gene having a NF- $\kappa$ B binding site; and

XXVIII. Claim 86, drawn to isolated or recombinant I $\kappa$ B.

**Applicants' reply**

In response, applicants hereby elect, with traverse, the Group which includes new claims 89 and 90, which appears to be Group XXIV. Applicants also respectfully request examination of at least new claims 89 and 90 if no other claims are rejoined upon consideration of applicants' reasons below for traverse of the March 28, 2006 restriction requirement.

Applicants respectfully traverse the March 28, 2006 restriction requirement because it is not in compliance with 35 U.S.C. §121 which permits restriction only if two or more independent and distinct inventions are claimed in one application. Under M.P.E.P. §803, the Examiner must examine the application on the merits, even though it includes claims to distinct inventions, if the search and examination of an application can be made without serious burden.

The purported inventions of Groups I-XXVIII are not independent. Under M.P.E.P. §802.01, "independent" means there is no disclosed relationship between the subjects disclosed. The inventions of the Groups all relate to a new transcription factor, NF- $\kappa$ B, which is common to all the claims. The Examiner's grouping of the claims merely separates specific examples of the use of applicants' new discovery into different groups. However,

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knowledge of NF- $\kappa$ B and its activity is common to all of the examples.

Furthermore, under M.P.E.P. § 803, the Examiner must examine the application on the merits if examination can be made without serious burden, even if the application would include claims to distinct or independent inventions. That is, there are two criteria for a proper requirement for restriction: 1) the invention must be independent and distinct, **and** 2) there must be a serious burden on the Examiner if restriction is not required.

Applicants respectfully submit that there would not be a serious burden on the Examiner if restriction is not required because a search of the prior art relevant to NF- $\kappa$ B would necessarily uncover any existing prior art relevant to each of the purported Groups. Since there is no burden on the Examiner to examine the Groups together in the subject application, the Examiner must examine the entire application on the merits.

In view of the foregoing, applicants maintains that restriction is not proper under 35 U.S.C. § 121 and respectfully requests that the Examiner reconsider and withdraw the requirement for restriction.



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**Supplemental Information Disclosure Statement**

In accordance with their duty of disclosure under 37 C.F.R. §1.555, Applicants direct the Examiner's attention to the following disclosures, which are listed on Form PTO-1449 (**Exhibit A**). Copies of all of the references listed have been submitted in connection with U.S. Patent No. 6,410,516 and its in reexamination proceedings (*Ex Parte* Reexamination Control Nos. 90/007,503, filed April 4, 2005, and 90/007,828, filed December 2, 2005). The subject application claims benefit of the filing date of U.S. Patent No. 6,410,561 under 35 U.S.C. §120. Accordingly, copies of items 1-375 are not attached to this Supplemental Information Disclosure Statement but are readily available to the Examiner and to the public from the file history of U.S. Patent No. 6,410,516.

1. U.S. Patent No. 5,804,374, issued September 8, 1998, Baltimore et al.;
2. U.S. Patent No. 6,150,090, issued November 21, 2000, Baltimore et al.;
3. File history of U.S. Serial No. 06/817,441, filed January 9, 1986;
4. File history of U.S. Serial No. 06/946,365, filed December 24, 1986;
5. File history of U.S. Serial No. 07/155,207, filed February 12, 1988;
6. File history of U.S. Serial No. 07/162,680, filed March 1, 1988;

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7. File history of U.S. Serial No. 07/280,173, filed December 5, 1988;
8. File history of U.S. Serial No. 07/318,901, filed March 3, 1989;
9. File history of U.S. Serial No. 07/341,436, filed April 21, 1989;
10. File history of U.S. Serial No. 07/791,898, filed November 13, 1991 Abandoned;
11. File history of U.S. Serial No. 08/418,266, filed April 6, 1995;
12. File history of U.S. Serial No. 08/463,397, filed June 5, 1995;
13. File history of U.S. Serial No. 08/464,364, filed June 5, 1995;
14. File history of U.S. Serial No. 08/959,160 filed October 28, 1997;
15. File history of U.S. Serial No. 10/037,341, filed January 4, 2002;
16. File history of U.S. Serial No. 10/037,415 filed January 4, 2002;
17. WO 92/20795, 26 Nov. 1992, PCT/US92/04073, filed 14 May 1992;

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19. Aoki, N., "Patenting Biological Pathways", Boston Globe (2002) pg. 1 and 3;
20. Auphan, N. et al., "Immunosuppression by Glucocorticoids: Inhibition of NF- $\kappa$ B Activity Through Induction of I $\kappa$ B Synthesis", Science (1995) 270:286-290;
21. Baeuerle, P., "NF- $\kappa$ B: Ten Years After", Cell, (1996) 87:13-20;
22. Baeuerle, P.A. "NF- $\kappa$ B as a Frequent Target For Immunosuppressive and Anti-Inflammatory Molecules", Advances in Immunology (1997) 55:111-137;
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No. 08/464,364, ADL 0000874-0000888, Document 198, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;

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08/464,364, ADL 0000924-0000953, Document 198-8, filed  
02/03/2006, in Civil Case 02 CV 11280 RWZ;

197. June 25, 2002 Complaint, 02 CV 11280 RWZ;

198. August 18, 2002 Declaration of Michael Karin (20 pgs),  
including Tabs 1-24, 02 CV 11280 RWZ;

199. August 19, 2002 Defendants Eli Lilly & Company Memorandum  
In Support Of Its Combined Motion To Dismiss Under  
Fed.R.Civ.P. 12(b)(6) and Motion for Summary Judgment of  
Invalidity Under 35 USC Section 102 and 112, including  
Exhibits A-D, 02 CV 11280 RWZ;

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202. October 16, 2002 Declaration of Brendan F. Boyce, M.B.  
Ch.B. including Tabs A-D, 02 CV 11280 RWZ;

203. October 16, 2002 Declaration of Dr. Thomas D. Gilmore  
including Exhibits A-C and D1-D24, 02 CV 11280 RWZ;

204. October 17, 2002 Plaintiffs Opposition to Defendants Eli  
Lilly & Com.'s Combined Motion to Dismiss Pursuant to  
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35 USC Sections 102 and 112 including Tabs A-M, 02 CV 11280  
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Fed.R.Civ.R.12(b)(6) And Motion For Summary Judgment of  
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- 210. August 20, 2003 Plaintiffs Ariad Pharmaceutical, Inc. et al. Response to Eli Lilly and Company's First Set of Rule 33 Interrogatories (Nos. 1-4);
- 211. September 5, 2003 Eli Lilly & Company's Responses to Plaintiffs First Set of Interrogatories (Nos. 1-5);
- 212. October 6, 2003 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Responses to Eli Lilly & Company's Second Set of Rule 33 Interrogatories (No. 5);
- 213. November 3, 2003 Tutorial Hearing, 02 CV 11280 RWZ;
- 214. November 3, 2003 Evidentiary Hearing before Honorable Rya W. Zobel, 02 CV 11280 RWZ;
- 215. November 24, 2003 Plaintiffs Opening Brief on Claim Construction, 02 CV 11280 RWZ;
- 216. November 24, 2003 Declaration of Laurie H. Glimcher, M.D.,;
- 217. November 24, 2003 Declaration of Vladimir V. Drozdoff in Support of Plaintiffs Opening Brief on Claim Construction, including Tabs 1-22, 02 CV 11280 RWZ;
- 218. November 24, 2003 Declaration of Dr. Thomas D. Gilmore, 02 CV 11280 RWZ;
- 219. November 24, 2003 Defendants Eli Lilly & Company Opening Claim Construction Brief (not signed), 02 CV 11280 RWZ, including Exhibits to Eli Lilly's Opening Claim Construction Brief, inc. Exhibits A-H and I & J, 02 CV 11280 RWZ;

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- 220. November 24, 2003 unsigned Defendant Eli Lilly and Company's Opening Claim Construction Brief, Document 198-3, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
- 221. December 22, 2003 Plaintiffs Opposition Brief on Claim Construction, 02 CV 11280 RWZ;
- 222. December 22, 2003 Declaration of Vladimir V. Drozdoff in Support of Plaintiffs Opposition Brief on Claim Construction, including Tabs 1-18, 02 CV 11280 RWZ;
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- 226. January 13, 2004 Markman Transcript Hearing before the Honorable Rya W. Zobel, U.S. District Judge, 02 CV 11280 RWZ;
- 227. January 13, 2004 Markman Hearing by Plaintiff, 02 CV 11280 RWZ;
- 228. January 13, 2004 Markman Hearing, A Scientific Tutorial by Eli Lilly & Comp. Paul H. Berghoff;
- 229. February 24, 2004 Motion For Leave To File Reply Memorandum

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- 230. March 3, 2004 Memorandum of Decision & Order re: Claim Construction, 02 CV 11280 RWZ;
- 231. March 3, 2004 Memorandum of Decision and Order, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
- 232. March 23, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ Albert S. Baldwin, Jr., Ph.D.;
- 233. March 24, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Supplemental Response to Eli Lilly & Company's First Set of Rule 33 Interrogatories (Nos. 1-5);
- 234. March 24, 2004 Eli Lilly & Company's Supplemental Response to Plaintiffs' First Set of Interrogatories (Nos. 1-5);
- 235. April 30, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Second Supplemental Response to Eli Lilly & Company's First Set of Rule 33 Interrogatories (Nos. 1-5);
- 236. April 30, 2004 Eli Lilly & Company's Second Supplemental Responses to Plaintiffs' First Set of Interrogatories (Nos. 1-5);
- 237. May 7, 2004 Subpoena in a Civil Case 02 CV 11280 RWZ Chen-Ming Fan Ph.D.;
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Michael J. Lenardo M.D.;

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Ranjan Sen Ph.D.;

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Responses to Eli Lilly & Company's Third Set of Rule 33  
Interrogatories (No. 6);

244. June 2, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al.  
Third Supplemental Response to Eli Lilly & Company's First  
Set of Rule 33 Interrogatories (Nos. 1-5);

245. June 7, 2004 Hearing before Honorable Rya W. Zobel, without  
Jury;

246. June 28, 2004 Deposition of Jonathan H. Lebowitz in Civil  
Case 02 CV 11280 RWZ including deposition Exhibits 5-11 and  
13 attached with this Supplemental Information Disclosure  
Statement, namely: October 28, 1987 correspondence from  
Barbara Bakal Greene [LeBowitz 6/28/04 Exh 5]; May 19, 1987  
Notice of Grant Award [LeBowitz 6/28/04 Exh 6]; July 26,  
1988 Notice of Grant Award [LeBowitz 6/28/04 Exh 7];  
December 19, 1989 Notice of Grant Award [LeBowitz 6/28/04

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Exh 8]; April 23, 1990 Notice of Grant Award [LeBowitz 6/28/04 Exh 9]; Set of hand written notes [LeBowitz 6/28/04 Exh 10]; Set of hand written notes [LeBowitz 6/28/04 Exh 11]; and Set of hand written notes [LeBowitz 6/28/04 Exh 13] (deposition Exhibits 2 and 14 are copies of the subject patent, deposition Exhibit 12 is plaintiffs' privileged log, and deposition Exhibits 1, 3 and 4 have been submitted as items 164, 2 and 167, respectively, in Patentees' August 8, 2005 Information Disclosure Statement);

247. June 30, 2004 Deposition of Harinder Singh, Ph.D. in Civil Case 02 CV 11280 RWZ including deposition Exhibits 21-25 attached with this Supplemental Information Disclosure Statement, namely: February 25, 1988 American Type Culture Collection [Singh 6/30/04 Exh 21]; Set of hand written notes [Singh 6/30/04 Exh 22]; Set of hand written notes [Singh 6/30/04 Exh 23]; Set of hand written notes [Singh 6/30/04 Exh 24] and Set of hand written notes [Singh 6/30/04 Exh 25] (deposition Exhibits 17, 18, 27, 28, 30 and 31 have been submitted as items 163, 1, 26, 27, 76 and 100, respectively in Patentees' August 8, 2005 Information Disclosure Statement);

248. August 23, 2004 Defendant's Exhibit 45 - Asserted Claims Against EVISTA;

249. August 23, 2004 Deposition of Dr. David Baltimore in Civil Case 02 CV 11280 RWZ;

250. August 23, 2004 Videotaped Deposition of Dr. David Baltimore, pgs. 1-4, and 85-87 in Civil Case 02 CV 11280 RWZ;



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251. September 30, 2004 Deposition of Dr. Phillip A. Sharp in Civil Case 02 CV 11280 RWZ including deposition Exhibits 87-89 attached with is Supplemental Information Disclosure Statement, namely: February 13, 1986 correspondence from Brian W. Kimes, Ph.D. [Sharp 9/30/04 Exh 87]; April 30, 1986 Notice of Grant Award [Sharp 9/30/04 Exh 88]; and November 3, 1986 Notice of Grant Award [Sharp 9/30/04 Exh 89] (deposition Exhibits 85 and 86 have been submitted as items 29 and 28 in Patentees' August 8, 2005 Information Disclosure Statement);
252. October 12, 2004 Deposition of Ranjan Sen in Civil Case 02 CV 11280 RWZ;
253. October 18, 2004 Eli Lilly & Company's Response to Plaintiffs' Second Set of Requests for Admission to Eli Lilly & Company (Nos. 19-23);
254. October 21, 2004 Deposition of Chen-Ming Fan in Civil Case 02 CV 11280 RWZ;
255. October 22, 2004 Deposition of Michael J. Lenardo, M.D. in Civil Case 02 CV 11280 RWZ;
256. October 26, 2004 Deposition of Albert S. Baldwin, Jr. Ph.D. in Civil Case 02 CV 11280 RWZ;
257. November 2, 2004 Eli Lilly & Company's Third Supplemental Responses to Plaintiffs First Set of Interrogatories (Nos. 1-5);
258. November 10, 2004 Deposition of Thomas P. Maniatis, Ph.D. in Civil Case 02 CV 11280 RWZ;

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- 259. November 12, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Responses to Eli Lilly & company's Fourth Set of Rule 33 Interrogatories (Nos. 7-8);
- 260. December 1, 2004 Deposition of Dr. Patrick Baeuerle in Civil Case 02 CV 11280 RWZ;
- 261. December 13, 2004 Defendant's Response to Plaintiffs Fourth Set of Interrogatories (Nos. 8-18);
- 262. December 15, 2004 Plaintiffs Ariad Pharm., Inc. et al. Responses to Eli Lilly & Com.'s First Set of Requests For Admission (Nos. 1-25), 02 CV 11280 RWZ;
- 263. December 15, 2004 Eli Lilly & Company's Responses to Plaintiffs' Third Set of Requests for Admission (Nos. 24-45);
- 264. December 15, 2004 Plaintiffs Ariad Pharmaceuticals, Inc. et al. Responses to Eli Lilly & Company's Fifth Set of Rule 33 Interrogatories;
- 265. March 14, 2005 Plaintiffs' Supplemental Response to Eli Lilly's Fourth Set of Rule 33 Interrogatories (Nos. 7-8);
- 266. March 14, 2005 Eli Lilly & Company's Response to Plaintiffs Fifth Set of Interrogatories;
- 267. June 6, 2005 Order Concerning Discovery & Stay of Proceedings, 02 CV 11280 RWZ;
- 268. September 7, 2005 Expert Report of Peter Barnes, Ph.D. in

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Civil Case 02 CV 11280 RWZ;

269. September 9, 2005 Expert Report of Dr. Laurie H. Glimcher in Civil Case 02 CV 11280 RWZ;
270. September 9, 2005 Expert Report of Dr. Laurie H. Glimcher, pages cover, 9, 14-15, and 32 in Civil Case 02 CV 11280 RWZ;
271. September 9, 2005 Expert Report of David Latchman, DSc., Ph.D., pgs. Cover, 5 and 11, in Civil Case 02 CV 11280 RWZ;
272. September 15, 2005 Plaintiffs' Third Supplemental Response to Eli Lilly & Company's First Set of Interrogatories (Nos. 1-4);
273. Expert Report of David Latchmann, Dsc., Ph.D., dated September 5, 2005, including copies of the following referenced in the report: Altavilla, Cardiovascular Research (2001) 52:143-152; January 13, 2004 Markman Hearing; November 2, 2003 Tutorial Hearing; Baldwin, Jr., Annu. Rev. Immunol. (1996) 14:649-81; Baltimore, Nature (1988) 335:395-396; Bielinska, Science (1990) 250:997-1000; Blackwell, Arthritis & Rheumatism (2004) 50:2675-2684; Blanco-Colio, Circulation (2000) 102:1020-1026; Böhnlein, Cell (1988) 53:827-836; Budhram-Mahadeo, The Journal of Biological Chemistry (1996) 271:9108-9113; Cavazzana-Calvo, Nature (2004) 427:779-781; Cross, Science (1989) 244:466-469; Dang, Clinical Cancer Research (1999) 5:471-474; Davis, Science (1991) 253:1268-1271; Fan, The EMBO Journal (1989) 8:101-110; Fawell, Proc. Natl. Acad. Sci. USA (1994) 91:664-668; Friedman, Nature (1988) 335:452-454; Goodbourn, Proc. Natl. Acad. Sci. USA (1988) 85:1447-1451; Hoag,

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275. Expert Report of Peter Barnes, Ph.D., dated September 9, 2005 including: Appendix B Baltimore Deposition; Appendix C Baldwin Deposition; January 13, 2004 Markman Hearing; November 3, 2003 Tutorial Hearing; Baeuerle, Cell (1996) 87:13-20; Baldwin, Jr. Annu. Rev. Immunol. (1996) 14:649-81; Barnes, D.M., D.Sc., The New England Journal of Medicine 1997 336:1066-1071; Beg, Nature, (1995) 376:167-170; Blackwell, Am. J. Respir. Cell Mol. Biol. (1997) 17:3-9; Brown, Proc. Natl. Acad. Sci. USA (1993) 90:2532-2536; Collins, The Journal of Clinical Investigation (2001) 107:255-264; Resume of Peter John Barnes; Han, The Journal of Biological Chemistry (1999) 274:939-947; Hoffman, Science (2002) 298:1241-1245; Ito, Nucleic Acids Research (1994) 22:3787-3792; Klement, Molecular and Cellular Biology (1996) 16:2341-2349; Li, J. Exp. Med. (1999) 11:1839-1845; Ariad et al. v. Eli Lilly and Company A Scientific Tutorial; Ariad et al. v. Eli Lilly and Company Markman Presentation; Noble, J. Exp. Med. (1996) 183:2373-2378; March 3, 2004 Memorandum of Decision and Order; Scott, Genes & Development (1993) 7:1266-1276; Selected pages of NF- $\kappa$ B Tutorial; and Sun, Science (1993) 259:1912-1915;

276. Expert Report of Stavros C. Manolagas, M.D., Ph.D., dated

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285. Expert Report of Dr. Stephen Prescott, dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-96 attached with this Fourth Supplemental Information Disclosure Statement, namely: U.S. Patent No. 6,410,516, issued June 25, 2002, Baltimore et al.; Physicians' Desk Reference, 24<sup>th</sup> Ed. (1970) various pages of the Generic and Chemical Name Index; Physicians' Desk Reference 39<sup>th</sup> Ed. (1985) pp.1811-1813; Declaration Under 37 C.F.R. §1.132 by David Baltimore signed September 14, 1999; Examiner's Amendment pps. 2-31; Adams and Teegarden, J. Nutr. (2004) 134:2948-2952; Aljada et al., The Journal of Clinical Endocrinology & Metabolism (1996) 84:3386-3389; Alroy et al., Molecular and Cellular Biology (1995) 15:5789-5799; Auphan et al., Science (1995) 270:286-290; Baeuerle and Baichwal, Advances in Immunology (1997) 65:111-137; Baldwin Jr., A.S., Annu. Rev. Immunol. (1996) 14:649-681; Bantel et al., Am. J. Gastroenterol (2000) 95:3452-3457; Bennett Jr. et al., JAMA (1963) 183:166-169; Bergmann et al., Am. J. Respir. Cell Mol. Biol. (2004) 30:555-563; Bergmann et al., Immunology (2004) 111:430-434; Berry et al., Experimental Cell Research (2002) 272:176-184; Björnström and Sjöberg, Molecular Endocrinology (2005) 19:833-842; Blanco-Colio et

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287. Rule 26(A)(2) Report of Bert Spilker, Ph.D., M.D. dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibit 1 attached with this Fourth Supplemental Information Disclosure Statement, namely: Biography of Dr. Bert Spilker;
288. Rule 26(A)(2) Rebuttal Report of George R. Stark, Ph.D., dated October 21, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-45 attached with this Fourth Supplemental Information Disclosure Statement, namely: U.S. Patent No. 6,060,310, issued May 9, 2000, Cho-Chung; File History of U.S. Serial No. 08/464,364, filed June 5, 1995; U.S. Patent No. 6,410,516, issued June 25, 2002, Baltimore et al.; File History of U.S. Serial No. 07/162,680, March

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289. October 28, 2005 Rule 26(A)(2) Rebuttal Report of Michael Sofocleous, pgs. Cover, 22 and 33, in Civil Case 02 CV 11280 RWZ;
290. November 10, 2005 Eli Lilly and Company's Sixth Supplemental Responses To Plaintiffs' First Set of Interrogatories (Nos. 1-5), pgs. 1-6, in Civil Case 02 CV 11280 RWZ;
291. Reply Expert Report of Peter Barnes, D.M. D.Sc. dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-4 attached with this Fourth Supplemental Information Disclosure Statement, namely: Adams et al., Cancer Research (1999) 59:2615-2622; Davis et al., Science (1991) 253:1268-1271; Current Opinion in Cell Biology (1993) 5:477-487; Schmitz et al. Trends in cell Biology (1991) 5:130-137;
292. Rule 26(A)(2) Reply Report of Brendan F. Boyce, M.D. not dated (November 11, 2005) in Civil Case 02 CV 11280 RWZ including Exhibits 1-23 attached with this Fourth Supplemental Information Disclosure Statement, namely: Berkowitz et al., the Journal of Biological Chemistry (2002) 277:24694-24700; Blum et al., the American Journal

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293. Reply Expert Report of Dr. Jesus Egido dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-7 attached with this Fourth Supplemental Information Disclosure Statement, namely: Bertelli et al., Drugs Exptl. Clin. Res. (1998) XXIV:133-138; Buffoli et al., JHC exPress (2005) pp. 2-33; Hai-Hong et al., Journal of the Fourth Military Medical University (2003) 24:923-925; Lee et al., J. Of Clinical Pharmacology (1998) 38:981-993; Kundu and Surh, Mutation Research (2004) 555:65-80; Leiro et al., International Immunopharmacology (2005) 5:393-406; Tsai et

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294. Reply Expert Report of Dr. Laurie H. Glimcher dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-18 attached with this Fourth Supplemental Information Disclosure Statement, namely: Reply Report of Laurie Glimcher; Brueckmann et al., Thromb. Haemost. (2003) 89:149-160; Brueckmann et al., Inflamm. Res. (2004) 53:528-533; Brun-Buisson et al., JAMA (1995) 274:968-974; Derhaschnig et al., Blood (2003) 102:2093-2098; Dhainaut et al., Thromb. Haemost (2003) 90:642-653; Bernard et al., Intensive Care Med. (2003) 29:894-903; Dhainaut et al., Crit. Care Med. (2004) 32[Suppl]:S194-S201; Joyce et al., The Journal of Biological Chemistry (2001) 276:11199-11203; Joyce et al., Crit. Care Med. (2002) 30[Suppl]:S288-S293; Kalil et al., Shock (2004) 21:222-229; Kinasewitz et al., Critical Care (2004) 8:R82-R90; Martin et al., N. Engl. J. Med. (2003) 348:1546-1554; Nick et al., blood (2004) 104:3878-3885; Opal et al., The Journal of Infectious Diseases (1999) 180:1584-1589; U.S. Patent Application No. US2003/0073632, Published April 17, 2003, Ciaccia et al.; XIGRIS drotrecogin alfa (activated) Drug Action 2pg.; XIGRIS drotrecogin alfo (activated) 1p.;
295. Reply Expert Report of David Latchman, DSc., Ph.D. dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-18 attached with this Fourth Supplemental Information Disclosure Statement, namely: Adams et al., Cancer Research (1999) 59:2615-2622; Davis et al., Science (1991) 253:1268-1271; Liou and Baltimore, Current Opinion in Cell Biology (1993) 5:477-487; Schmitz et al. Trends in Cell Biology (1991) 1:130-137;

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296. Rule 26(B)(2) Reply Report of David M. Livingston, M.D. not dated (November 11, 2005) in Civil Case 02 CV 11280 RWZ including Exhibits 1-23 attached with this Fourth Supplemental Information Disclosure Statement, namely: Brueckmann et al., *Inflamm. Res.* (2004) 53:528-533; Brun-Buisson et al., *JAMA* (1995) 274:968-974; Chen et al. *Nature* (1998) 391:410-413; Deraschnig et al., *Blood* (2003) 102:2093-2098; Dhainaut et al., *thromb. Haemost* (2003) 90:642-653; Bernard et al., *Intensive Care Med.* (2003) 29:894-903; Dhainaut et al., *Crit. Care Med.* (2004) 32[Suppl]:S194-S201; Joyce et al., *The Journal of Biological Chemistry* (2001) 276:11199-11203; Joyce and Grinnell, *Crit. Care Med.* (2002) 30[Suppl]:S288-S293; Kalil et al. *Shock* (2004) 21:222-229; Kinasewitz et al., *Critical Care* (2004) 8:R82-R90; Marino et al., *Molecular and Cellular Endocrinology* (2001) 182:19-26; Martin et al., *N. Engl. J. Med.* (2003) 348:1546-1554; Müller and Harrison, *FEBS Letters* (1995) 369:113-117; Nick et al., *Blood* (2004) 104:3878-3885; Opal et al., *The Journal of Infectious Diseases* (1999) 180:1584-1589; Reifel-Miller et al., *The Journal of Biological Chemistry* (1994) 269:23861-23864; Control No. 05-A-1610-ASBMR; U.S. Patent Application No. US2003/0073632, Published April 17, 2003, Ciaccia et al.; U.S. Patent No. 5,393,763, issued February 28, 1995, Black et al.; U.S. Patent No. 6,545,027, issued April 8, 2003, Berg et al.; XIGRIS drotrecogin alfa (activated) Drug Action 2pg.; XIGRIS drotrecogin alfa (activated) Emerging Understanding 1pg.;
297. Reply Expert Report of Stavros C. Manolagas, M.D., Ph.D. Regarding Invalidity of the Asserted Claims dated November 11, 2005 in Civil Case 02 CV 11280 RWZ including Exhibits 1-11 attached with this Fourth Supplemental Information

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300. November 11, 2005 Reply Expert Report of Dr. Jeffrey Ravetch, pgs. 1-11, in Civil Case 02 CV 11280 RWZ;
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302. November 11, 2005 Reply Expert Report of David Latchman, DSc., Ph.D., Document 198, filed 02/03/2006, pgs. 1-58, in Civil Case 02 CV 11280 RWZ;
303. November 18, 2005 Condensed Deposition of Carolyn Smith in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-11 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Carolyn Louise Smith, Ph.D., ADL Bates Nos. 0037187-0037205 [DDX 300 11/18/05]; September 8, 2005 Expert Report of Dr. Carolyn L. Smith Restricted Confidential [DDX 301 11/18/05]; November 11, 2005 Declaration of Carolyn Smith [DDX 302 11/18/05]; Laboratory notebook of Dr. Carolyn Smith, Bates Nos. CLS 00001-00295 Confidential Information Under Protective Order [DDX 303 11/118/05]; Cavarretta, et al., Molecular Endocrinology (2002), 16(2):253-270 [DDX 304 11/18/05]; Coleman, et al., The Journal of Biological

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304. November 21, 2005 Plaintiffs' Supplemental Responses To Eli Lilly & Co.'s First, Second, Third, and Fourth Sets of Interrogatories (Nos. 2, 3, 6-8), in Civil Case 02 CV 11280 RWZ;
305. November 22, 2005 Condensed Deposition of Stephen Prescott in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-29 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum vitae of Stephen Michael Prescott [DDX 312]; October 21, 2005 Expert Report of Dr. Stephen Prescott [DDX 313]; (the Reply Expert Report of Dr. Stephen Prescott [DDX314] is being submitted under separate cover); November 11, 2005 Reply Expert Report of Stavros C. Manolagas, M.D., Ph.D. Regarding Invalidity of the Asserted Claims [DDX 315]; U.S. Patent No. 6,410,516 B1, issued June 25, 2002, Baltimore et al. [DDX 316]; Tsoukas, Science, (2004), 224:1438-1440 [DDX 317]; Manolagas, et al., Journal of Clinical Endocrinology and Metabolism, (1986), 63(2):394-400 [DX318]; Lemire et al., The Journal of Immunology, (1985), 134(5):3032-3035 [DX319]; Lemire et al., Rapid Publication, (1984), 74:657-



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307. December 9, 2005 Condensed Deposition of George Stark in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-20 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum vitae of George R. Stark, Ph.D. [DDX 356 12/9/05]; October 21, 2005 Rule 26(A)(2) Rebuttal Report Of George R. Stark, Ph.D. [DDX357 12/9/05]; September 9, 2005 Expert Report of David Latchman, DSc., Ph.D. [DDX358 12/9/05]; November 11, 2005 Reply Expert Report Of David Latchman, DSc., Ph.D. [DDX359 12/9/05]; September 9, 2005 Expert Report of Peter Barnes, Ph.D. [DDX360 12/9/05]; File History of U.S. Serial No. 07/341,436, filed April 21, 1989 [DDX370 12/9/05]; Horuk, R., Journal of Immunological Methods, (1989), 119:255-258 [DDX371 12/9/05]; Scott and Smith, Science, (1990), 249:386-390 [DDX372 12/9/05]; File History of U.S. Serial No. 07/280,173. Filed 12/05/88 [DDX373 12/9/05]; Khaled et al., Clinical Immunology and Immunopathology, (1998), 56:170-179 [DDX374 12/9/05]; Tomita et al., J. Hypertens, (1998), 16:993-1000 [DDX375 12/9/05]; Du et al., Molecular

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308. December 9, 2005 Deposition of Dr. George Stark, Document 198, filed 02/03/2006, pgs. 1-5, 128-129, 134-135, 147-148 and 277, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

309. December 12, 2005 Condensed Deposition of Jesus Egido in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-8 attached with this Third Supplemental Information Disclosure Statement, namely: Pasaje de los Aucionos, 24, 28034 Madrid [Egido 1 12/12/05]; Abbreviated Curriculum Vitae of Jesus Egido MD [Egido 2 12/12/05]; September 9, 2005 Expert Report-Dr. Jesus Egido [Egido 3 12/12/05]; Binder of references for J. Edigo which includes: St. Leger et al., The Lancet, (1979), 1017-1020; Manna et al., The Journal of Immunology (2000), 164:6509-6519; Holmes-McNary and Baldwin Jr., Cancer Research (2000), 60:3477-3483; Blanco-Colio, Circulation., (2000), 102:1020-1026; Department of Health & Human Services Public Health  
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311. December 13, 2005 Confidential Deposition of Peter Barnes, pp. 1-2, 48-49, 181-182 in Civil Case 02 CV 11280 RWZ;
312. December 14, 2005 Condensed Deposition of David Latchman in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-

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315. December 17, 2005 Condensed Deposition of Brendan F. Boyce Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-12 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Brendan Franceis Boyce [DDX 400 12/17/05]; Gianni et al., J. Clin. Endocrinol Metab., (2004), 89:6097-6099 [DDX403 12/17/05]; Blum, et al., The American Journal of Cardiology Brief Reports, (2000), 86:892-895 [DDX404 12/17/05]; Walsh et al., The American Journal of Cardiology, (2001), 88:825-828 [DDX405 12/17/05]; Jimi et al., Nature Medicine (2004), 10:617-624 [DDX406 12/17/05]; Compston, J.E., Physiological Reviews, (2001), 31:419-447 [DDX407 12/17/05]; Chadwick et al., PNAS, (2005), 102:2543-2548 [DDX408 12/17/05]; Harnish, et al., Endocrinology, (2000), 141:3403-3411 [DDX409 12/17/05]; U.S Patent No. 6,545,027 B1, issued April 8, 2003, Berg et al. [DDX410 12/17/05]; Reifel-Miller et al., The Journal of Biological Chemistry, (1994), 269:23861-23864 [DDX411 12/17/05]; Chen et al., Nature, (1998), 391:410-413 [DDX415 12/17/05]; Olivier, et al., Presentation Number: SU104 [DDX414 12/17/05];

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317. December 20, 2005 Videotaped Deposition of Thomas R. Kadesch, pgs. 1-4, 138, 196, 269, 297-299, 307-308 and 332, Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
318. December 22, 2005 Condensed Transcript of Videotaped Deposition of Stavros C. Manolagas in Civil Case 02 CV 11280 RWZ including deposition Exhibits 1, and 3-19 attached with this Supplemental Information Disclosure Statement, namely: September 9, 2005 Expert Report of Stavros C. Manolagas [Manolagas 12/22/05 Exh 1]; November 11, 2005 Reply Expert Report of Stavros C. Manolagas, M.D. Ph.D. Regarding Invalidity of the Asserted Claims [Manolagas 12/22/05 Exh 3]; Declaration of Stavros Manolagas, M.D. Ph.D. [Manolagas 12/22/05 Exh 4]; Curriculum Vitae of Stavros C. Manolagas, M.D., Ph.D. last

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319. December 22, 2005 Videotaped and Oral Deposition of Stavros C. Manolagas, pgs. 1-3, and 208-209, Document 198, filed 02/03/2006 in Civil Case 02 CV 11280 RWZ;
320. December 23, 2005 Condensed Deposition of David M. Livingston Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-6 attached with this Third Supplemental



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321. December 23, 2005 Declaration of Lawrence R. Robins In Support Of Defendant Eli Lilly and Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102 including Exhibits 1-13 in Civil Case 02 CV 11280 RWZ;
322. December 23, 2005 Declaration of Lawrence R. Robins in Support of Defendant Eli Lilly and Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, including Exhibits A-N in Civil Case 02 CV 11280 RWZ;
323. December 23, 2005 Defendant Eli Lilly and Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§ 101 and 112, First Paragraph in Civil Case 02 CV 11280 RWZ;
324. December 23, 2005 Defendant Eli Lilly and Company's Memorandum In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102 in Civil Case 02 CV 11280 RWZ;
325. December 23, 2005 Defendant Eli Lilly and Company's Motion

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326. December 23, 2005 Defendant Eli Lilly and Company's Rule 56.1 Statement In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102 in Civil Case 02 CV 11280 RWZ;
327. December 23, 2005 Memorandum In Support of Defendant Eli Lilly And Company's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph filed under seal pursuant to parties' stipulated protective order in Civil Case 02 CV 11280 RWZ;
328. December 23, 2005 Defendant's Rule 56.1 Statement In Support of Its Motion for Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph in Civil Case 02 CV 11280 RWZ;
329. January 17, 2006 Eli Lilly and Company's Renewed Motion To Stay This Litigation Pending Reexamination of the '516 Patent-In Suit in Civil Case 02 CV 11280 RWZ;
330. January 17, 2006 Memorandum In Support of Eli Lilly and Company's Renewed Motion To Stay This Litigation Pending Reexamination of the '516 Patent-In Suit including Exhibits A-T in Civil Case 02 CV 11280 RWZ;
331. January 25, 2006 Condensed Deposition of Robert Lindsay Civil Case 02 CV 11280 RWZ including deposition Exhibits 1-14 attached with this Third Supplemental Information Disclosure Statement, namely: Curriculum Vitae of Robert Lindsay [Lindsay 1 1/25/06]; March 3, 2004 Memorandum of

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Decision And Order [Lindsay 4 1/25/06]; December 21, 2005 Eli Lilly and Company To Pay U.S. \$36 Million Relating To Off-Label Promotion [Lindsay 5 1/25/06]; Cosman and Lindsay, Endocrine Reviews, (1999), 20:418-434 [Lindsay 6 1/25/06]; Kousteni et al., J. Clin. Invest. (2003), 111:1651-1664 [Lindsay 7 1/25/06]; Helvering et al., Molecular Pharmacology, (2005), 63:1225-1238 [Lindsay 8 1/25/06]; 71.-77. Of deposition [Lindsay 9 1/25/06]; Walsh et al., the American Journal of Cardiology, (2001), 88:825-828 [Lindsay 10 1/25/06]; Gianni, et al., J. Clin. Endocrinol. Metab., (2004), 89:6097-6099 [Lindsay 11 1/25/06]; Blum et al., The American Journal of Cardiology, (2000), 86:892-895 [Lindsay 12 1/25/06]; U.S. Patent NO. 4,418,068, issued November 29, 1983, Jones [Lindsay 13 1/25/06]; Bone and Health and Osteoporosis: A Report of the Surgeon General 2004, Executive Summary <[http://www.surgeongeneral.gov/library/bonehealth/Executive\\_summary.html](http://www.surgeongeneral.gov/library/bonehealth/Executive_summary.html)> [Lindsay 14 1/25/06]; Bone Health and Osteoporosis Chapter 9 pp219-253 [Lindsay 15 1/25/06]; U.S. Patent No. 6,545,027 B1, issued April 8, 2003, Berg et al. [Lindsay 16 1/25/06];

332. January 31, 2006 Declaration of Peter Barlett Bressler, M.D., Document 198, filed 02/03/2006 in Civil Case 02 CV 11280 RWZ;

333. January 31, 2006 Plaintiffs' Memorandum In Opposition To Eli Lilly and Company's Renewed Motion To Stay This Litigation Pending Reexamination Of the '516 Patent-In Suit including Exhibits 1-7 and 8A-8I, Document 194, filed 01/31/2006, in Civil Case 02 CV 11280 RWZ;

334. February 1, 2006 First Declaration of Jeffrey V. Ravetch,

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MD, Ph.D., Document 198, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

335. February 1, 2006 Second Declaration of Jeffrey Ravetch M.D., Ph.D., Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

336. February 3, 2006 Concise Statement of Material Facts As to Which There Is A Genuine Issue In Support Of Plaintiff's Opposition To Lilly's Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102, Document 202, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

337. February 3, 2006 Declaration of Vladimir V. Drozdoff In Support of Plaintiffs' Opposition to Defendant Eli Lilly & Co.'s Motion For Summary Judgment of Invalidity Under 35 U.S.C. section 102 and Related Documents, Document 203, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

338. February 3, 2006 Declaration of Vladimir V. Drozdoff in Support of Plaintiffs' Opposition to Defendant Eli Lilly & Co.'s Motion For Summary Judgment of Invalidity Under 35 U.S.C. Section 101 and 112, First Paragraph, Document 200, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

339. February 3, 2006 Plaintiffs' Opposition to Defendant Eli Lilly & Co.'s Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph filed under seal, Document 198-1, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;

340. February 4, 2006 Plaintiffs' Memorandum In Opposition To Defendant Eli Lilly & Co.'s Motion For Summary Judgment of

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Invalidity Under 35 U.S.C. Section 102 filed under seal,  
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RWZ;

341. February 24, 2006 Declaration of Leslie A. McDonell in Support of Defendant Eli Lilly and Company's Reply Memorandum In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §102, Document 214-1, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
342. February 24, 2006 Declaration of Leslie A. McDonell in Support of Defendant Eli Lilly and Company's Reply Memorandum In Support of Its Motion For Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 211, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
343. February 24, 2006 Motion For Leave To File Reply Memorandum In Support Of Defendant Eli Lilly and Company's Motion For Summary Judgment Of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 210-1, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
344. February 24, 2006 Reply Memorandum In Support of Defendant's Motion For Summary Judgment Of Invalidity Under 35 U.S.C. §102, Document 213-2, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;
345. February 24, 2006 Reply Memorandum In Support of Defendant's Motion for Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 210-2, filed 02/24/2006, in Civil Case 02 CV 11280 RWZ;

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346. March 3, 2006 Plaintiffs' Opposition To Defendant Eli Lilly & Co.'s Motion For Leave To File A Reply Brief In Support of its Summary Judgment of Invalidity Under 35 U.S.C. Section 102 including Exhibit 1, Document 218, filed 03/03/2006, in Civil Case 02 CV 11280 RWZ;
347. March 3, 2006 Concise Statement Of Material Facts As To Which There Is A Genuine Issue In Support of Plaintiffs Opposition to Defendant Eli Lilly & Company's Motion for Summary Judgment of Invalidity Under 35 U.S.C. §§101 and 112, First Paragraph, Document 199, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ;
348. March 3, 2006 Plaintiffs Opposition to Defendant Eli Lilly & Company's Motion For Leave To File Reply Memorandum In Support Of Eli Lilly and Company's Motion for Summary judgment of Invalidity under 35 U.S.C. §§101 and 112, First Paragraph, Document 217, filed 03/03/2006, in Civil Case 02 CV 11280 RWZ;
349. March 12, 2006 Condensed Transcript of Videotaped Deposition of Stavros Manolagas, M.D., Ph.D. Vol. II in Civil Case 02 CV 11280 RWZ including deposition Exhibits 22-33 attached with this Supplemental Information Disclosure Statement, namely: Helvering et al., Pharmacol (2005) Vol. 68, No. 5, pp. 1225-1238 [Manolagas 03/12/06 Exh 22]; Taranta et al., Bone (2002) Vol. 30, No. 2, pp. 368-376 [Manolagas 03/12/06 Exh 23]; Expert Report of Jeffrey V. Ravetch, M.D., Ph.D. [Manolagas 03/12/06 Exh 24]; Yu, X-P. et al., Proc. Natl. Acad. Sci, USA (1995) 92:10990-10994 [Manolagas 03/12/06 Exh 25]; Manolagas et al., J. Clin. Endocrinal Metab (1986) Vol. 63, No. 2, pp. 394-400 [Manolagas 03/12/06 Exh 26]; Tsoukas, Science

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(1984) 224:1438-1440 [Manolagas 03/12/06 Exh 27]; Galdiero et al., Microbiology (2001) 147:2697-2704 [Manolagas 03/12/06 Exh 28]; Yang et al., Nature (1998) 395:284-288 [Manolagas 03/12/06 Exh 29]; Prager, Eur. J. Haematology (1997) 59:162-170 [Manolagas 03/12/06 Exh 30]; Lamon-Fava et al., Arterioscler Thromb Vasc Biol. (1999) 19:2960-2965 [Manolagas 03/12/06 Exh 31]; Marino et al., Molecular and Cellular Endocrinology (2001) 182:19-26 [Manolagas 03/12/06 Exh 32]; Reifel-Miller et al., The Journal of Biological Chemistry (1994) 269:23861-23864 [Manolagas 03/12/06 Exh 33];

- 350. Trial Transcript - April 10, 2006 Jury Trial Day 1, First Session pgs. 1-61, Word Index pgs. 1-10, Second Session pgs. 62-115, Word Index pgs. 1-12, in Civil Case 02 CV 11280 RWZ;
- 351. Trial Transcript - April 11, 2006 Jury Trial Day 2, First Session pgs. 1-66, Word Index 1-13, Second Session pgs. 66-131, Word Index 1-13, in Civil Case 02 CV 11280 RWZ;
- 352. Trial Transcript - April 12, 2006 Jury Trial Day 3, First Session pgs. 1-67, Word Index 1-12, Second Session pgs. 68-125, Word Index 1-10, in Civil Case 02 CV 11280 RWZ;
- 353. Trial Transcript - April 13, 2006 Jury Trial Day 4, First Session pgs. 1-71, Word Index 1-12, Second Session pgs. 72-1128, Word Index 1-10, in Civil Case 02 CV 11280 RWZ;
- 354. Trial Transcript - April 14, 2006 Jury Trial Day 5, First Session pgs. 1-71, Word Index 1-13, Second Session pgs. 72-122, Word Index 1-10, in Civil Case 02 CV 11280 RWZ;

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- 355. Trial Transcript - April 18, 2006 Jury Trial Day 6, First Session pgs. 1-91, Word Index 1-16, Second Session pgs. 92-171, Word Index 1-16, in Civil Case 02 CV 11280 RWZ;
- 356. Trial Transcript - April 19, 2006 Jury Trial Day 7, First Session pgs. 1-106, Word Index 1-18, Second Session pgs. 107-174, Word Index 1-14, in Civil Case 02 CV 11280 RWZ;
- 357. Trial Transcript - April 20, 2006 Jury Trial Day 8, First Session pgs. 1-89, Word Index 1-14, in Civil Case 02 CV 11280 RWZ;
- 358. Trial Transcript - April 20, 2006 Jury Trial Day 8, Second Session pgs. 90-157, in Civil Case 02 CV 11280 RWZ;
- 359. April 20, 2006 Complaint For Declaratory Judgment of Patent Invalidity And Non-Infringement, *Amgen, Inc. et al. V. Ariad Pharmaceuticals, Inc.*, Civil Case 06 CV 00259- KAJ;
- 360. Trial Transcript - April 21, 2006 Jury Trial Day 9, First and Second Sessions pgs. 1-143, in Civil Case 02 CV 11280 RWZ;
- 361. Trial Transcript - April 24, 2006 Jury Trial Day 10, First and Second Session pgs. 1-152 and Word Index pgs. 1-22, in Civil Case 02 CV 11280 RWZ;
- 362. Trial Transcript - April 25, 2006 Jury Trial Day 11, First and Second Session pgs. 1-158 and Word Index pgs. 1-25, in Civil Case 02 CV 11280 RWZ;
- 363. Trial Transcript - April 26, 2006 Jury Trial Day 12, First and Second Session pgs. 1-156 and Word Index pgs. 1-14,



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Second Session pgs. 88-156 and Word Index pgs. 1-14, in  
Civil Case 02 CV 11280 RWZ;

- 364. Trial Transcript - April 27, 2006 Jury Trial Day 13, First  
Session pgs. 1-86, in Civil Case 02 CV 11280 RWZ;
- 365. Trial Transcript - April 27, 2006 Jury Trial Day 13, Second  
Session pgs. 88-141, in Civil Case 02 CV 11280 RWZ;
- 366. Trial Transcript - April 28, 2006 Jury Trial Day 14, First  
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130, Word Index 1-17, in Civil Case 02 CV 11280 RWZ;
- 367. Jury Questions - April 2, 2006 pgs. 1-27, Word Index pgs.  
1-5, in Civil Case 02 CV 11280 RWZ;
- 368. Jury Questions - April 3, 2006 pgs. 1-7, Word Index pgs. 1-  
2, in Civil Case 02 CV 11280 RWZ;
- 369. Transcript of Verdict of Jury Trial, Day 18, May 4, 2006  
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- 370. M. Grieve, Garlic, Botanical.com [online], [retrieved on  
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<URL:http://www.botanical.com/botanical/mgmh/g/garlic06.h  
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[retrieved on 2002-08-16], retrieved from the Internet:

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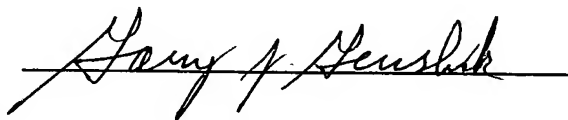
373. Bayer, Questions and Facts, {online}, [retrieved on-unknown];

374. Undated Declaration of Stavros Manolagas, M.D. Ph.D. in Reexamination Control No. 90/007,503, Document 201, filed 02/03/2006, in Civil Case 02 CV 11280 RWZ; and

375. Claims from U.S. Serial No. 07/341,438, filed April 21, 1989, in Civil Case 02 CV 11280 RWZ.

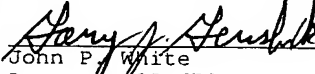
No fee, other than the enclosed \$1,205.00 for a five-month extension of time and excess claim fee is deemed necessary in connection with the filing of this Amendment. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to:  
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 9/28/06  
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Gary J. Gershik  
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